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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|------------------------|-----------------------------|------------------|
| 10/016,282 | 12/06/2001 | Thomas W. Konownalchuk | LFT000 CIP3 | 4202 |
| 7590 02/08/2005 Thomas W. Konownalchuk 1070 NE 7th Drive Newport, OR 97365 | | | EXAMINER HUI, SAN MING R | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1617 | |

DATE MAILED: 02/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|--------------------------------------|---|--|
| Office Action Summary | Application No. 10/016,282 | Applicant(s) KONOWALCHUK ET AL. | |
| | Examiner San-ming Hui | Art Unit 1617 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 November 2004.
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9,12-18 and 20-26 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 1-9,12-18 and 20-26 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 9, 2004 has been entered.

The cancellation of claims 10, 11, and 19 is acknowledged. Claims 1-9, 12-18, and 20-26 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9, 12-18, and 20-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "synergistic combination" recited in claims 1, 9, 17, and 26 renders the claims indefinite because it is not clear what combination between the alcohols or diols and the acids would produce a synergistic combination. The instant specification does not define what a "synergistic combination" would be.

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The amendments filed November 9, 2004 amends the claims so that the instant claims are directed to a method of inactivating a virus by a composition consisting essentially of a carrier and a synergistic combination of alcohols or diols and an acid. Examiner considers the rejections under 35 USC 103 (a) set forth in the previous office action as properly reject the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-6, 9, 12-14, 16-18, 20-23, and 25-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et al. (US Patent 5,385,938) in view of Poli et al. (Food Chemistry, 1979; 4(3): 251-258), Wenninger (International Cosmetic Ingredient Dictionary and Handbook, 7th ed., Vol. 1, page 163-168), and Merck Index (11th ed., 1989, Glycolic acid monograph 4394, page 4399).

Yu et al. teaches a topical composition with glycolic acid is the active and about 12.4% ethanol as solvent (See col. 14, Example 1). Yu et al. also teaches that the composition has pH of 3.0 (See col. 14, Example 1). Yu et al. also teaches that the glycolic acid composition is useful to eradicate lesions such as warts, which is a viral infection of papillomas virus (See col. 30, line 10 – col. 31, line 2). Yu et al. also teaches that other pharmaceutically acceptable vehicles other than water and ethanol may be used (See col. 13, lines 11-13). Yu et al. also teaches that the concentration of

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hydroxyacids, including glycolic acid, may range from 0.02 to 12M (See col. 13, lines 17-19). Yu et al. also disclosed that the amphoteric compounds are not necessarily present in the composition of Yu et al. in order to have antiviral activities (See col. 11, lines 55-59). Yu et al. also teaches that the composition may be formulated into gel, ointment, cream, lotion, and other cosmetic and pharmaceutical preparation (See col. 13, lines 4-6).

Yu et al. does not expressly teach 1,3-butanediol, as known as butylenes glycol, is useful as pharmaceutical vehicle. Yu et al. does not expressly teach that the glycolic acid containing topical composition as useful in the prophylaxis of lesions caused by viruses within the Herpesviridae. Yu et al. does not expressly teach the composition having a specific pH of 2.45. Yu et al. does not expressly teach the concentration of glycolic acid in the composition as 0.6%.

Poli et al. teaches that glycolic acid is virucidal against herpesvirus (See particularly page 253, Table 1).

Wenninger teaches that butylenes glycol as useful as solvent in numerous cosmetic marketed products (See page 163-168).

Merck Index teaches that the pH 0.5% of glycolic acid solution as 2.50 (See the glycolic acid monograph). Examiner notes that 0.5% of glycolic acid is about 0.31M.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ butylenes glycol as solvent in the topical wart-treating composition of Yu et al. and adjust the pH to 2.45. It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the glycolic acid

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containing topical composition, in the prophylaxis of lesions caused by viruses within the Herpesviridae. It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate 0.6% of glycolic acid to the herein claimed prophylactic method.

One of ordinary skill in the art would have been motivated to employ butylenes glycol as solvent in the topical wart-treating composition of Yu et al. and adjust the pH to 2.45 because butylenes glycol is known to be useful in cosmetic products as solvent. Employing any known solvents, including butylene glycol, into a topical composition would have been reasonably expected to be useful in formulating a topical wart-treating composition and treating the same. Moreover, the optimization of result effect parameters (e.g., pH of the composition and the amount of active (glycolic acid)) is obvious as being within the skill of the artisan since 0.31M is within the range disclosed in Yu et al., absent evidence to the contrary.

One of ordinary skill in the art would have been motivated to employ the glycolic acid containing topical composition in the prophylaxis of lesions caused by viruses within the Herpesviridae. Based on the teachings of Poli et al. and Yu et al., glycolic acid is known to be effective in killing herpes virus. Therefore, applying a glycolic acid composition to reduce the number of herpes viruses, and thereby reducing the chances for herpes viruses to cause the lesions, would have been reasonably expected to be effective.

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Claims 1, 7-8, 15, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bhatia et al. (Indian Journal of Animal Sciences 1998; 68(6): 518-520, reference of record) in view of Disinfectant Drugs (Therapeutic Products Programme Guidelines published by Health Canada, April 1999, pages 42-45) and Remington (Remington's Pharmaceutical Sciences, 18th ed., 1990, pages 218-219 and 1314-1315).

Bhatia et al. teaches that 0.4N hydrochloric acid is effective in inactivating sheep pox virus (See particularly page 519, col. 1, Table 1 and col. 2, third paragraph). Bhatia et al. also teaches that the "Ranch" strain of goat pox virus is more sensitive in acidic pH 3.0 as there was 5 log fall in the titer in the acidic pH (See page 519, col. 2, third paragraph).

Bhatia et al. does not expressly teach the use of hydrochloric acid with an alcohol, in the amount of 0.2% to 30% or 0.2% to 12.5% in volume, in the method of prophylaxis of lesions caused by Poxviridae such as molluscum contagiosum. Bhatia et al. does not expressly teach the pH of the composition as 2.45.

Disinfectant Drugs teaches isopropanol 15% or above is effective as a single medicinal ingredient for disinfecting contact lens (See page 43, Table).

Remington teaches that isopropanol is a very good pharmaceutical solvent, which is comparable to ethanol (see page 219, col. 1). Remington also teaches that ethanol is a very good pharmaceutical solvents (See page 1314, col. 2 – page 1315, col. 1).

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It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate isopropanol, in the amount of 0.2% to 30% or 0.2% to 12.5% in volume, with hydrochloric acid in a method for the prophylaxis of lesions caused by Poxviridae such as molluscum contagiosum. It would have been obvious to one of ordinary skill in the art at the time the invention was made to adjust the pH of the composition to 2.45.

One of ordinary skill in the art would have been motivated to incorporate isopropanol, in the amount of 0.2% to 30% or 0.2% to 12.5% in volume, with hydrochloric acid in a method for the prophylaxis of lesions caused by Poxviridae such as molluscum contagiosum because isopropanol is known to be useful as both a solvent and a disinfectant and hydrochloric acid is known to have virucidal activities against pox viruses. Employing hydrochloric acid in a method of prophylaxis of lesions caused by pox viruses, such as molluscum contagiosum, would have been reasonably expected to be effective. Incorporating a well-known commonly used pharmaceutical solvent, such as isopropanol, into a topical formulation and optimizing the amount of such solvent used for the same purpose would be obvious as being within the purview of skilled artisan. Moreover, adding a secondary disinfectant such as isopropanol to control the secondary infection which may be accompanied by the outbreaks or lesions caused by such virus infection would also be reasonably expected to be useful. Furthermore, optimization of the pH to 2.45 would be considered obvious as being within the purview of skilled artisan.

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It is applicant's burden to demonstrate unexpected results over the prior art. See MPEP 716.02, also 716.02 (a) - (g). Furthermore, the unexpected results should be demonstrated with evidence that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992). Moreover, evidence as to any unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). In the instant case, the data in page 9, 10, 14-16 has been considered, but are not found persuasive. The data merely demonstrates the upper limit of effective pH for virucidal activities. Please note that the pH of the composition mainly depend on the amount of acids present in the composition. Therefore, the data regarding the pH limitation is considered as a reflection of what the effective amount of glycolic acid required in order for the composition to be virucidal (See page 10 of the instant specification, Tables 2 and 3). This is seen to be an expected effect based on the cited prior art. No convincing and clear unexpected result is seen.

Response to Arguments

Applicant's rebuttal arguments filed November 9, 2004 averring the amphoteric compounds, which are required to be in the composition in order to produce an pH of 2.45, being excluded by the claims as amended have been considered, but are not found persuasive. The claims herein are given the broadest reasonable interpretation.

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The herein claimed method of prophylaxis of viral infection employs a composition having an alcohol and an acid. Although in the pH of the particular example of Yu without the pseudoamphoteric compound is 1.9, Yu teaches the effective amount of glycolic acid can be in the range of 0.02 to 12M (See col. 13, lines 17-19). As discussed in the rejections above, when the concentration of glycolic acid is about 0.31 M, the pH is about 2.5, which falls within the herein claimed range. Moreover, Yu et al. clearly disclosed that the amphoteric compounds are not necessarily present in the composition of Yu et al. in order to have antiviral activities (See col. 11, lines 55-59). Furthermore, even arguing, the amphoteric compounds can be considered as a pH adjusting agents which are pharmaceutical carriers and are allowed in the composition (See for example, page 13, second-to-last paragraph, the instant specification). Therefore, whether the composition "consisting essentially of" or "consisting of" the herein claimed components (i.e., carrier, alcohol or diol, and acid), the cited prior arts render the instant claims obvious.

Applicant's rebuttal arguments file November 9, 2004 averring the cited prior art's failure to teach glycolic acid as effective in prophylaxis for lesions caused by herpes virus, have been considered, but are not found persuasive. Although the cited prior art not expressly teaches the prophylaxis effectiveness, based on the teachings of Poli et al. and Yu et al., glycolic acid is known to be effective in killing herpes virus. Therefore, applying a glycolic acid composition to reduce the number of herpes viruses, and thereby reducing the chances for herpes viruses to cause the lesions, would have been reasonably expected to be effective.

Applicant's rebuttal arguments file November 9, 2004 averring the cited prior art's failure to provide motivation to incorporate 1,3-butanediol into the herein claimed method, have been considered, but are not found persuasive. 1,3-butanediol is known as a commonly used solvent for pharmaceutical use. In other words, 1,3-butanediol is a well-known pharmaceutically acceptable carrier. Incorporating such commonly used solvent in pharmaceutical art into the pharmaceutical composition of Yu for treatment or prophylaxis of viral infection would be obvious as the selection of one or another commonly used solvent would be seen as a simple selection from among obvious alternatives.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In the instant case, the motivation to combine based on the fact that hydrochloric acid is known to be effective in against goat-pox virus and isopropanol is a well-known solvent and disinfectant. Combining these two agents for very same purpose would be obvious, absent evidence to the contrary.

Applicant's rebuttal arguments file November 9, 2004 averring the cited prior art's failure to provide motivations or suggestion to combine isopropanol and hydrochloric

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acid have been considered, but are not found persuasive. The motivation lies in that hydrochloric acid is known to be effective in against goat-pox virus and isopropanol is a well-known solvent and disinfectant. Combining these two agents for very same purpose would be obvious, absent evidence to the contrary.

Applicant's rebuttal arguments filed November 9, 2004 averring Bhatia not teaching the herein claimed method of prophylaxis for lesions caused by herpes and/or pox viral infection have been considered, but are not found persuasive. Although the cited prior art not expressly teaches the prophylaxis effectiveness, based on the teachings of Bhatia et al., hydrochloric acid is known to be effective in killing pox virus. Therefore, applying a hydrochloric acid composition to reduce the number of pox viruses, and thereby reducing the chances for pox viruses to cause the lesions, would have been reasonably expected to be effective.

Applicant's rebuttal arguments filed November 9, 2004 averring Bhatia merely teaching the *in vitro* employment of hydrochloric acid and isopropanol to kill goat-pox viruses and therefore, not suggest the herein claimed method of prophylaxis for lesions caused by herpes and/or pox viral infection have been considered, but are not found persuasive. Since both hydrochloric acid is known to be effective in against goat-pox virus and isopropanol is a well-known solvent and disinfectant, the employment of both agents would have been reasonably expected to exert the very same antiviral effect, and thus, useful as effective prophylaxis of pox viruses thereby. The teachings of the Bhatia demonstrates that the herein claimed active agents as effective in killing the

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goat-pox virus, regardless of when such agent is applied, absent evidence to the criticality as to the timing of application or viral contact to the herein claimed agent.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



San-ming Hui
Primary Examiner
Art Unit 1617